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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,544	09/10/2003	Hidenobu Senpuku	242617US0	3249

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EXAMINER
GRUN, JAMES LESLIE

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
08/28/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/658,544	SENPUKU ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 20 July 2007 has been entered. Claims 2-8 remain in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The disclosure remains objected to because of the following informalities: the specification is replete with grammatical, idiomatic, and spelling errors too numerous to be specifically listed and should be carefully revised. Appropriate correction is required.

The specification is objected to and claims 2-8 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record as containing subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth, any correlative relationship between IgA antibodies at a single time point and caries risk is purely speculative and unpredictable according to applicant's own teachings, as well as those of the prior art (see e.g. Acton et al. (Hum. Immunol. 60: 984, 1999) or Thylstrup et al. (Textbook of Clinical Cariology,

page 405)), because determining the quantity of *Streptococcus mutans* in human saliva does not correlate with caries risk for a number of reasons. Therefore, as set forth, one would question applicant's possession of the invention as disclosed and/or claimed and one would not be assured of the ability to practice the invention as disclosed and/or claimed absent further written description and guidance from applicant. Note that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement. Also, the disclosure, not the knowledge of one skilled in the art, must supply the novel aspects of an invention for adequate enablement.

Applicant's arguments filed 20 July 2007 have been fully considered but they are not deemed to be persuasive for the reasons of record. Notwithstanding applicant's assertions to the contrary, determining the quantity of *Streptococcus mutans* in human saliva at a single time point is the only measure put forth in the instant specification for correlating the level of IgA antibodies to caries risk, a measure that applicant and the prior art teach is not very useful for assessing caries risk.

The specification is objected to and claims 2-8 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth, absent further written description and guidance from applicant, one would question

applicant's possession of the invention as now claimed and one would not be assured of the ability to practice the invention as now claimed because applicant describes and teaches the peptide consisting of SEQ ID NO: 2 (see, e.g., pages 8 and 11) as the relevant antigen for determination of patient saliva immunoglobulin A specific therefor, not the peptide consisting of SEQ ID NO: 1, as is now claimed, a peptide which is instead taught as a MHC class II molecule-binding epitope (see pages 7-8), not as one for detection of antibody binding. Again, applicant is requested to direct the Examiner's attention to specific passages where support for these newly recited limitations can be found in the specification as filed or is required to delete the new matter.

Applicant's arguments filed 20 July 2007 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, the sequence of amino acid residues 361-386 of the surface protein antigen of *Streptococcus mutans* (PAc) is listed as SEQ ID NO: 2, not SEQ ID NO: 1.

The specification is objected to and claims 2-8 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record, set forth with regard to the previous similar subject matter of claims 5-8, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As set forth, the specification, as originally filed, does not provide support for the secretory immunoglobulin A (IgA) being labeled.

Applicant's arguments filed 20 July 2007 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

Claims 2-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "low" and "high" in claim 2 are relative terms which render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Moreover, in claim 2 and claims dependent thereupon, it is not clear if one or more antibodies are intended and, if more than one is intended, which is directed against antigen.

In claim 5 and claims dependent thereupon, it is not clear if anything in the independent claim is being further limited because it is not clear if one or more antibodies are intended and, if more than one is intended, if one or both are labeled.

Applicant's arguments filed 20 July 2007 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, the claims remain unclear and applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

Should applicant amend the claims to claim the determination of antibodies to the peptide as disclosed, the following would become applicable:

Claims 2-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Gregory (US 2003/0113823), Matsushita et al. (Inf. Imm. 62: 4034, 1994), Senpuku et al. (Scand. J. Immunol. 54: 109, 2001), and Kaneko et al. (J. Dental Health 52: 450, 2002).

Gregory teaches the determination of future dental caries activity in a human by determination of secretory IgA antibodies in saliva from the human specific for particular cell attachment antigens of *Streptococcus mutans*, including IgA antibodies specific for the antigen I/II thereof. Rapid tests, as well as enzyme-linked immunosorbent assays with saline-diluted saliva, are taught (see e.g. page 7). In contrast to the invention as instantly disclosed, the reference does not teach linear epitopes in the A-region of the antigen I/II which bind the salivary IgA antibodies.

Matsushita et al. determined IgA antibodies specific for a recombinantly produced (r) surface protein antigen of *S. mutans* (PAc, also known as antigen I/II, P1, B, SR, IF, or MSL-1) in the saliva of humans (see e.g. Fig. 2B). Moreover, the reference determined linear epitopes in the A-region of PAc which bound the salivary IgA antibodies (see Fig. 4). The reference teaches that antibodies in saliva were similar in reactivity pattern, albeit different in titer, to those found in the serum of the same donor (see Figs. 3 and 4; and, page 4037), and that human sera reacted with the peptide consisting of amino acid residues 363-373 of PAc (see Figs. 3-5 and page 4040), or amino acid residues 319-328 of PAc (see Figs. 3 and 4; and, page 4037). Implicitly, antibodies that bind to a short linear peptide (amino acid residues 363-373 of PAc) entirely

contained within a longer linear peptide (amino acid residues 361-386 of PAc), which do not depend upon a terminal amino or carboxyl group for binding, also bind to the longer peptide.

Senpuku et al. teach amino acid residues 365-377 of *Streptococcus mutans* PAc as a linear epitope relevant to the cell attachment function of PAc.

Kaneko et al. teach the correlation of antibodies specific for amino acid residues 361-386 of *Streptococcus mutans* PAc with the level of dental caries.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have determined secretory IgA antibodies in saliva from human patients specific for linear epitopes in the A-region of the antigen I/II (i.e. PAc), particularly in the region of amino acid residues 361-386, in the method of Gregory because Gregory teaches the determination of future dental caries activity in a human by determination of secretory IgA antibodies in saliva from the human specific for particular cell attachment antigens of *S. mutans*, including IgA antibodies specific for the antigen I/II thereof, and Matsushita et al., Senpuku et al., and Kaneko et al. teach a linear region of the antigen I/II (i.e. PAc) cell attachment antigen of *S. mutans* which binds antibodies in human patients that are indicative of a risk of dental caries, and which is involved in the attachment function of the protein.

It would have been further obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted any conventional label on the detection antibodies of Gregory and/or Matsushita et al., as modified, because one would have had obvious motivation and a reasonable expectation that any alternative label would successfully perform the detection function and such substitution is an obvious matter of design choice depending upon signal detection preference.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JLG/
James L. Grun, Ph.D.
August 16, 2007

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